Serum cholesterol levels do not influence outcome or recovery in acute ischemic stroke

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Abstract

OBJECTIVE: To examine the influence of admission serum cholesterol levels (SCL) on severity of initial neurological deficit, neurological outcome at month 3 and neurological recovery in patients with acute first-ever ischemic stroke. METHODS: Prospectively collected data from 889 consecutive patients with first-ever acute ischemic stroke were retrospectively analysed. Patients who suffered a recurrent ischemic stroke (n=22) or died (n=30) during the follow-up period were excluded from this study. Age, gender, arterial hypertension, diabetes mellitus, smoking, stroke etiology, SCL and severity of neurological deficit, using the National Institute of Health Stroke Scale (NIHSS), at presentation (NIHSS0) and after 3 months (NIHSS1), were assessed. Neurological recovery was defined as difference in NIHSS score (ΔNIHSS), according to ΔNIHSS = NIHSS0 - NIHSS1. RESULTS: Data from 837 patients (66% men, age: 62 +/- 14 years) were analysed. NIHSS1 was 2.3 +/- 1.8 and ΔNIHSS was 3.4 +/- 3. Clinically insignificant correlations between SCL and NIHSS0 (r=-0.13, p=0.0002), NIHSS1 (r=-0.09, p=0.001) and ΔNIHSS (r=-0.1, p=0.03) were evident. Multivariate binary logistic regression analysis revealed smoking (p=0.008), stroke etiology (p=0.023) and NIHSS0 (p<0.001) but not age, gender, arterial hypertension, diabetes mellitus or SCL as predictors for ΔNIHSS. CONCLUSION: Our data suggest that SCL in patients with acute ischemic stroke are not associated with neurological deficit on admission, outcome or neurological recovery.
Serum cholesterol levels do not influence outcome or recovery in acute ischemic stroke

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Abstract

Background and Purpose: We examined the influence of admission serum cholesterol levels (SCL) on severity of initial neurological deficit, neurological outcome at 3 months and neurological recovery in patients with acute first-ever ischemic stroke.

Methods: Prospectively collected data from 889 consecutive patients with first ever acute ischemic stroke were retrospectively analyzed. Patients who suffered a recurrent ischemic stroke (n=22) or died (n=30) during the follow-up period were excluded from this study. Age, sex, arterial hypertension, diabetes mellitus, smoking, stroke etiology, SCL, and severity of neurological deficit, using the National Institute of Health Stroke Scale (NIHSS), at presentation (NIHSS<sub>0</sub>) and after three months (NIHSS<sub>1</sub>) were assessed. Neurological recovery was defined as difference in NIHSS score (Δ<sub>NIHSS</sub>), according to Δ<sub>NIHSS</sub> = NIHSS<sub>0</sub> - NIHSS<sub>1</sub>.

Results: Data from 837 patients, 66% men, age 62±14 years was analyzed. NIHSS<sub>1</sub> was 2.3±1.8 and Δ<sub>NIHSS</sub> 3.4±3. Clinically insignificant correlations between SCL and NIHSS<sub>0</sub> (r= -0.13, p=0.0002), NIHSS<sub>1</sub> (r= -0.09, p=0.001) and Δ<sub>NIHSS</sub> (r= -0.1, p=0.03) were evident. Multivariate binary logistic regression analysis revealed smoking (p=0.005), stroke etiology (p=0.005) and NIHSS<sub>0</sub> (p<0.001) but not age, gender, arterial hypertension, diabetes mellitus or SCL as predictors for Δ<sub>NIHSS</sub>.

Conclusions: Our data suggest that SCL in patients with acute ischemic stroke are not associated with neurological deficit on admission, outcome or neurological recovery.

(200 words)
**Introduction**

Several studies described an influence of brain nutrients—specifically glucose and cholesterol—on outcome in patients with acute ischemic stroke. High serum glucose levels are unanimously considered markers of adverse outcome [1]. Up to date, two studies have examined the potential influence of serum cholesterol levels (SCL) on outcome in patients with acute ischemic stroke; one described a better outcome in patients with higher admission SCL [2], while the second reported a decreased mortality following acute ischemic stroke in patients taking lipid lowering agents at stroke onset [3]. The purpose of this study was to evaluate the hypothesis that SCL influence the clinical course of acute stroke patients. We therefore examined the relation between SCL and (1) severity of neurological deficit on admission, (2) neurological outcome at 3 months and (3) neurological recovery in patients with first-ever ischemic stroke.

**Patients and Methods**

Prospectively collected data from 889 consecutive patients with first ever acute ischemic stroke admitted in our neurological department between August 1997 and December 2004 were retrospectively analyzed for this study. Patients enrolled in therapeutic trials, patients who suffered a recurrent ischemic stroke (n=22) or patients who died (n=30) during the follow-up period were excluded from this study. Diagnostic work-up Cranial CT (CCT) was performed in all patients on admission. 12-lead ECG and ultrasound evaluation of the brain supplying arteries[4] were performed in all, and brain MRI, 24-h ECG monitoring and transthoracic or transesophageal (TEE) echocardiography in selected cases.
The following clinical characteristics were assessed: Age; sex; arterial hypertension defined by pre-admission history and medical records; diabetes mellitus defined either as fasting venous plasma glucose concentration of $\geq 7.0$ mmol/l after an overnight fast on at least two separate occasions, or as venous plasma glucose concentration of $\geq 11.1$ mmol/l following the ingestion of 75 g of oral glucose during the 2-h test; smoking; total venous SCL from blood drawn within 48 hours after symptom onset with the patient in supine position; severity of neurological deficit, using the National Institute of Health Stroke Scale (NIHSS), at presentation (NIHSS$_0$) and after three months (NIHSS$_1$). Stroke etiology was defined according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification[5] as (1) atherothrombotic in patients with a $>$50% stenosis or occlusion of the supplying cerebral artery. Patients with aortic plaques with a diameter of $\geq 4$ mm or mobile aortic thrombi located before the ostium of the left subclavian artery on TEE, but no other potential stroke etiology were also assumed to have an atherothrombotic etiology of stroke (2) cardioembolic in patients with a potential cardiac embolic source, (3) lacunar in patients who presented with one of the traditional clinical lacunar syndromes and either normal CT / MRI or a relevant subcortical or brain stem lesion with a diameter $< 1.5$ cm, (4) stroke of other defined etiology and (5) stroke of undetermined etiology, when no, or more than one potential etiologies were found.

Statistical analysis

A standard software package (SPSS 12.0) was used for statistical analysis. Quantitative variables were expressed as mean±standard deviation (SD). Significance was declared at $p < 0.05$.

Neurological recovery was defined as difference in NIHSS score ($\Delta_{\text{NIHSS}}$), according to

$$\Delta_{\text{NIHSS}} = \text{NIHSS}_0 - \text{NIHSS}_1.$$
recovery ($\Delta$NIHSS) and functional outcome (NIHSS$_1$) were examined using Pearson correlation. For multivariate binary logistic regression analysis with backward elimination of non-significant predictors, patients were divided into 2 groups of either $\Delta$NIHSS $\leq$ 0 (worsening or no clinical improvement during follow up) or $>$ 0 (improvement during follow up). Age (continuous variable), gender, SCL (continuous variable), diabetes mellitus (yes/no), arterial hypertension (yes/no), smoking (yes/no), stroke etiology (cardioembolic/ atherothrombotic/ lacunar/ other known/ unknown etiology) and NIHSS$_0$ (continuous variable) served as possible predictors. Since the relationship between $\Delta$NIHSS and SCL was the main interest of this study, latter variable was kept in the model, even if not significant.

**Results**

Data from 837 patients, 66% men, age 62±14 years (mean±SD, minimum 16, maximum 90 years) was analyzed. Arterial hypertension was found in 526 (63%) and diabetes mellitus in 128 (15%) patients. NIHSS$_0$ score was 6±5 (mean±SD; minimum 0, maximum 40). Etiology of stroke was atherothrombotic in 238 (28%), cardioembolic in 156 (19%), lacunar in 181 (22%), other determined etiology in 82 (10%) and undetermined in 210 (25%) patients. NIHSS$_1$ was 2.3±1.8 (mean±SD; minimum 0, maximum 22) and $\Delta$NIHSS 3.4±3 (mean±SD; minimum -7, maximum 28). Clinically insignificant correlations between SCL and NIHSS$_0$ ($r$= -0.13, $p$=0.0002), NIHSS$_1$ ($r$= -0.09, $p$=0.009; Figure 1) and $\Delta$NIHSS ($r$=-0.1, $p$=0.03, all Pearson test) were evident.

Multivariate binary logistic regression analysis with backward elimination of non-significant predictors revealed smoking ($p$=0.005), stroke etiology ($p$=0.005) and NIHSS$_0$
(p<0.001) but not age (p=0.995), gender (p=0.79), arterial hypertension (p=0.4), diabetes mellitus (p=0.96) and SCL (p=0.89) as predictors for $\Delta_{\text{NIHSS}} \leq 0$ or $> 0$ (Table 1).
Discussion

A previous study demonstrated a worse outcome in patients with admission SCL $< 6.5$ mmol/l, as compared to remaining patients at one month follow-up[2]. The present study could not confirm this finding: even though the correlations between SCL and the clinical measures ($\text{NIHSS}_0$, $\text{NIHSS}_1$, $\Delta\text{NIHSS}$) were statistically significant, the low $r$-values suggest that this result is of no clinical relevance. The reason for the discrepancy between our results and those of the previous paper could be methodological differences, particularly concerning duration of follow-up (one month in the previous and three in our study) and dichotomization of SCL at 6.5 mmol/l. It could be argued that our failure to reproduce the results of the former study was simply due to the lower number of enrolled patients. However, the results of our statistical analysis were clear-cut and did not demonstrate trends for clinically relevant effects of SCL. We refrained from dichotomizing our data using a specific SCL value as cut-off point, as this statistical method is clearly inferior to the multivariate model applied.

In conclusion, our data suggest that SCL in patients with acute ischemic stroke are not associated with neurological deficit on admission, outcome or neurological recovery.
References


Table 1: Evaluation of independent predictors of neurological recovery at three months ($\Delta_{\text{NIHSS}}$) using multivariate binary logistic regression analysis in 837 patients with first-ever acute ischemic stroke.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.0</td>
<td>0.98-1.02</td>
<td>0.99</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>1.1</td>
<td>0.68-1.65</td>
<td>0.79</td>
</tr>
<tr>
<td>Diabetes mellitus (yes/no)</td>
<td>0.98</td>
<td>0.55-1.76</td>
<td>0.96</td>
</tr>
<tr>
<td>Arterial hypertension (yes/no)</td>
<td>0.82</td>
<td>0.53-1.29</td>
<td>0.4</td>
</tr>
<tr>
<td>Smoking (yes/no)</td>
<td>0.54</td>
<td>0.36-0.83</td>
<td>0.005</td>
</tr>
<tr>
<td>Stroke etiology*</td>
<td>1.23</td>
<td>1.1-1.43</td>
<td>0.005</td>
</tr>
<tr>
<td>SCL (mmol/l)</td>
<td>0.99</td>
<td>0.84-1.17</td>
<td>0.89</td>
</tr>
<tr>
<td>NIHSS₀</td>
<td>1.52</td>
<td>1.36-1.7</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*: (cardioembolic/ atherothrombotic/ lacunar/ other known etiology/ unknown etiology)
Figure 1: Relationship between SCL and neurological outcome at 3 months following acute ischemic stroke.